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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,239	11/03/2003	Andrew S. Pekosz	60005161-0114	3764

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SONNENSCHEIN NATH & ROSENTHAL LLP
P.O. BOX 061080
WACKER DRIVE STATION, SEARS TOWER
CHICAGO, IL 60606-1080

EXAMINER	
SALVOZA, M FRANCO G	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/700,239	PEKOSZ ET AL.	
	Examiner	Art Unit	
	M. Franco Salvoza	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 95-98* is/are pending in the application.

4a) Of the above claim(s) *95 and 97* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25, 96, 98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 01, 2006 has been entered.

Election/Restrictions

Applicant's election with traverse of protein species PA in the reply filed on August 14, 2006 is acknowledged. The traversal is on the ground(s) that the Office has not established proper grounds for restriction; has not provided separate classification or status; the claims refer to cells which lack at least one or all nucleocapsid proteins; thus the assertion that these proteins have utility in a single combination is of no consequence to the scope of the claims under examination.

This is not found persuasive because the combination of the cell lacking all nucleocapsid proteins is structurally distinct from the combination of the cell lacking certain nucleocapsid proteins, each of which has structurally independent and distinct features and utility as a subcombination within the entire polymerase complex. Thus, the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and the subcombination has utility by itself or in other combinations (See MPEP § 806.05(c)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 95, 97 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 14, 2006.

Claims 1-25, 96, 98 are pending and under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 96 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a method for detecting the presence, absence or quantity of a segmented negative strand RNA virus in a biological sample suspected of comprising the virus, the method comprising providing a genetically engineered vertebrate cell comprising a recombinant RNA molecule that comprises an artificial segment of a segmented negative strand RNA virus or the complement thereof, the artificial segment comprising a 5' untranslated region of a segment, a reporter gene encoding a polypeptide and a 3' UTR of a segment.

It is unclear to what the "5' untranslated region of a segment" or "a 3' UTR of a segment" refers. It is not clear what applicant intends by "of a segment" or to which "segment" it refers.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25, 96, 98 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inclusion of entire 5' and 3' UTRs in recombinant RNA molecules, does not reasonably provide enablement for any fragments or any portions of these 5' and 3' UTRs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 P 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988) and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

In this case, the breadth of the claims, the amount of direction or guidance presented, the presence or absence of working examples, the state of the prior art are most relevant.

As indicated above, claim 1 broadly recites providing a genetically engineered vertebrate cell comprising a recombinant RNA molecule that comprises an artificial segment of a

segmented negative strand RNA virus or the complement thereof, the artificial segment comprising a 5' untranslated region (UTR) of a segment, a reporter gene encoding a polypeptide, and a 3' UTR of a segment. Claim 10 recites a cDNA of a 5' untranslated region (UTR), a reporter gene encoding a polypeptide, and a cDNA of a 3' UTR.

These recitations to "comprising a 5' UTR of a segment," "a 3' UTR of a segment," "a cDNA of a 5' UTR" or "a cDNA of a 3' UTR" also read on 5' and 3' UTR segments from "any" segments as well as "any" fragments of these UTR regions as well.

The art indicates the necessity of 3' and 5' UTR regions for influenza as providing conserved binding sites, poly A signals, and motifs for proper expression (See Szymkowiak et al., "Rapid method for the characterization of 3' and 5' UTRs of influenza viruses"). However, among the viruses and segments, certain portions are conserved, but the segments also contained significant nonconserved sequences.

Applicant's disclosure does contain examples such as Example 5, presumably teaching the entire UTR portion of the NP segment. However, the specification does not provide guidance as to minimum portions or conserved sequences of these UTR regions or any UTR regions of any segments that are necessary or must be conserved in order to ensure proper functioning and expression of the reporter gene as recited in the invention.

Thus, the disclosure does not sufficiently teach beyond entire portions of these UTR regions to counter the teachings in the art and enable the full scope of the claims which encompass fragments of these regions.

In view of these factors, the application has not provided sufficient information to enable those in the art to practice the claimed invention without undue experimentation.

Claims 1-25, 96, 98 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

See the Wands factors elucidated above for factors to weigh to make a determination of whether an application has met the requirements for enablement.

In this case, the most relevant factors are the amount of direction or guidance presented; the presence or absence of working examples, the state of the prior art.

As indicated above, claim 1 recites a method for detecting the presence, absence or quanity of a segmented negative strand RNA virus in a biological sample comprising providing a cell comprising a recombinant RNA molecule comprising a 5' UTR, a reporter gene, a 3' UTR, wherein the cell lacks at least one nucleocapsid protein of the virus.

References reviewing the state of the art for these particular diseases indicate that the minimal set of proteins required for transcription and replication of viral RNAs in the nuclei of infected cells include PA, PB1, PB2 and NP. (See Klumpp et al., "Roles of the influenza virus polymerase and nucleoprotein in forming a functional RNP structure,"; Lee et al., "Definition of the minimal viral components required for the initiation of unprimed RNA synthesis by influenza virus RNA polymerase"; Portela et al., "The influenza virus nucleoprotein: a multifunctional RNA-binding protein pivotal to virus replication") Further, while the art was not settled in regards to the necessity of including the PB2 protein, the more recent art teaches its inclusion

(See Perales et al., "The Influenza A Virus PB2 Polymerase Subunit Is Required for the Replication of Viral RNA").

Applicant's disclosure does contain a recitation to embodiments wherein the formation of translatable mRNA can occur even in the absence of a viral nucleocapsid protein in the cell prior to infection (p. 10). This is only further supplemented by Examples such as 1, 4, 5 teaching examples using the full complement of minimally required nucleocapsid proteins for expression of the reporter gene to indicate influenza virus activity. These examples, and the rest of the specification, do not indicate wherein the cell lacks at least one nucleocapsid protein or one of PA, NP, PB1 and PB2 and still indicates virus detection through expression of the reporter gene. Thus, the disclosure does not sufficiently teach beyond these few examples to counter the teachings in the art.

In view of these factors, the application has not provided sufficient information to enable those in the art to practice the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

WITHDRAWN

Claims 10-16, 19-23 and 25 were rejected under 102(b) as being anticipated by U.S. Patent No. 6,270,958 to Olivo et al.

Applicant contends that Olivo et al. does not recite all the elements of the claims by virtue of the amended claims reciting and utilizing cells lacking one or more proteins considered by Olivo et al. to be necessary for a virus detection assay.

Further, applicant contends that Nakagawa et al. cited in support does not teach expression of a polypeptide encoded by a reporter gene in response to infection of a cell; and

further that Nakagawa et al. does not address translation. Thus, Olivo et al. does not teach each and every element of any of claims 10-16, 19-23 and 25 even in view of Nakagawa 95' and 96'.

First, Olivo et al. supplements a teaching of nucleocapsid proteins with the caveat that the assay requires only the nucleocapsid proteins that are necessary and sufficient for replication of the minigenomes.

However, the more recent prior art post Nakagawa 95 and 96 indicates that for replication for the influenza virus genome, PB2 is indeed required for the replication of viral RNA. (See Perales et al., "The Influenza A Virus PB2 Polymerase Subunit Is Required for the Replication of Viral RNA," Journal of Virology, Vol. 71, No. 2, pp. 1381-1385 (1997)).

Thus, applicant's arguments are found persuasive and the rejection is withdrawn.

Claim Rejections - 35 USC § 103

WITHDRAWN

Claims 1-3, 6-9 and 18 were rejected under 35 U.S.C. 103(a) as unpatentable over Olivo in view of online dictionary.

Claim 24 was rejected under 35 U.S.C. 103(a) as unpatentable over Olivo et al. in view of Neumann et al.

Claims 4-5, 16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Olivo in view of Fodor et al.

Applicant contends that the Office has not demonstrated a reasonable expectation of success; Olivo et al. teaches each of the nucleocapsid proteins; thus, Olivo et al. does not disclose all the elements of the claimed methods.

Further Neumann et al. does not describe a method detecting a virus which involves cells lacking at least one nucleocapsid protein of the virus.

Further Fodor et al. does not describe a method detecting a virus which involves cells lacking at least one nucleocapsid protein of the virus.

Thus, neither Olivo et al. nor the other references either alone or in combination teach all the elements of said claims.

Based on the withdrawal of the rejection to the base reference of Olivo et al. (see ***Claim Rejections - 35 USC § 102*** above), applicant's arguments are considered and found persuasive, and the rejection is withdrawn.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

M. Franco Salvoza
Patent Examiner

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600